Whole-Brain Approaches for Investigating Iron Accumulation by R2* show no Excess from Occupational Exposure to Welding Fumes

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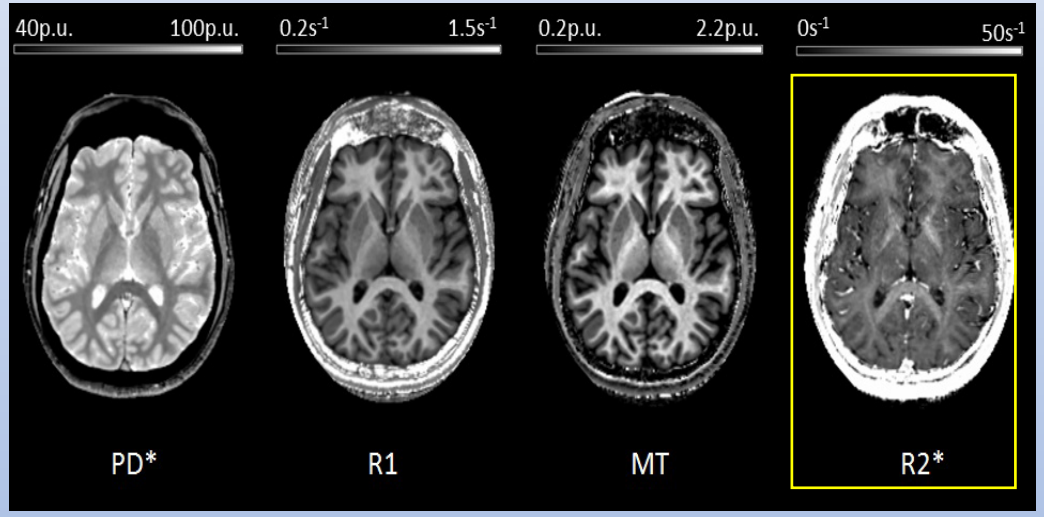
Background

- Iron (Fe) is a component in the Earth's crust
- Welding fumes are comprised of a mixture of heavy metal particulates including Fe and Mn
- Once inhaled, Fe and Mn can accumulate in the brain
- Fe and Mn compete for common transporters in the brain
- While Fe is found in elevated quantities in the human brain afflicted by neurodegenerative diseases, while Mn is a known neurotoxin that can lead to a disorder similar to Parkinson's Disease
  - Fe is known to induce oxidative stress, leading to cell death.

Background

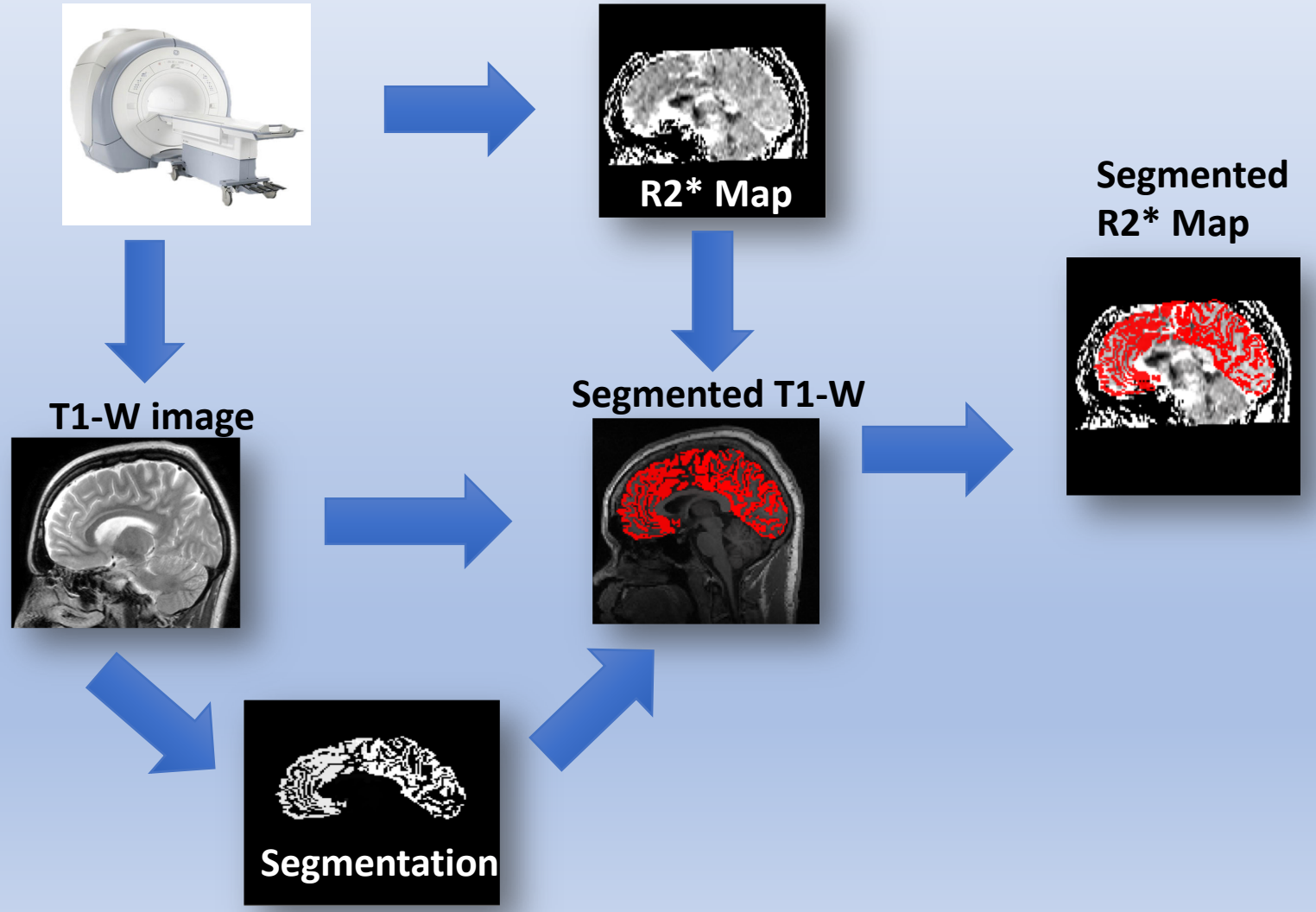
- Magnetic resonance imaging (MRI) can detect metals in the brain.
- R1 and R2* are MRI parameters that are proportionate to Mn and Fe accumulation, respectively
- Goal: to discriminate, using machine learning, between welders and controls using whole-brain R2* mapping.
- Hypothesis: There are characteristic differences between welders and controls in R2* based on Fe intake through occupational exposures.



http://www.fil.ion.ucl.ac.uk/Research/physics_info/QuantMRI_VBM.html

Previous: Materials and Methods

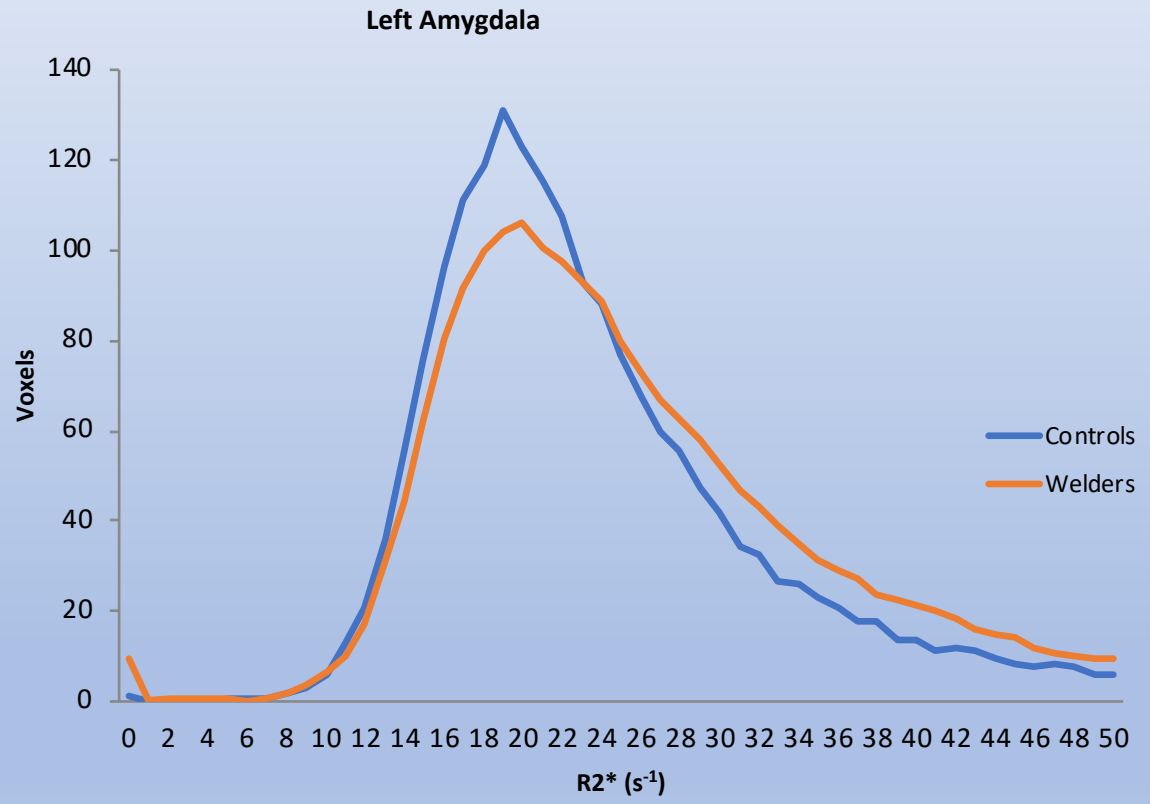
- 52 welders and 37 controls
- All scans were acquired using 3T GE MRI scanner
  - A spoiled gradient echo sequence with 6 echoes was used to obtain a R2* map
  - 3D T1-weighted FSPGR structural images were constructed
- Full-brain images segmented creating ROI masks using Freesurfer
- Coregistered whole-brain R2* maps with T1 weighted structural images using SPM12
- Using ROI masks, extracted R2* values from each ROI for use in data processing



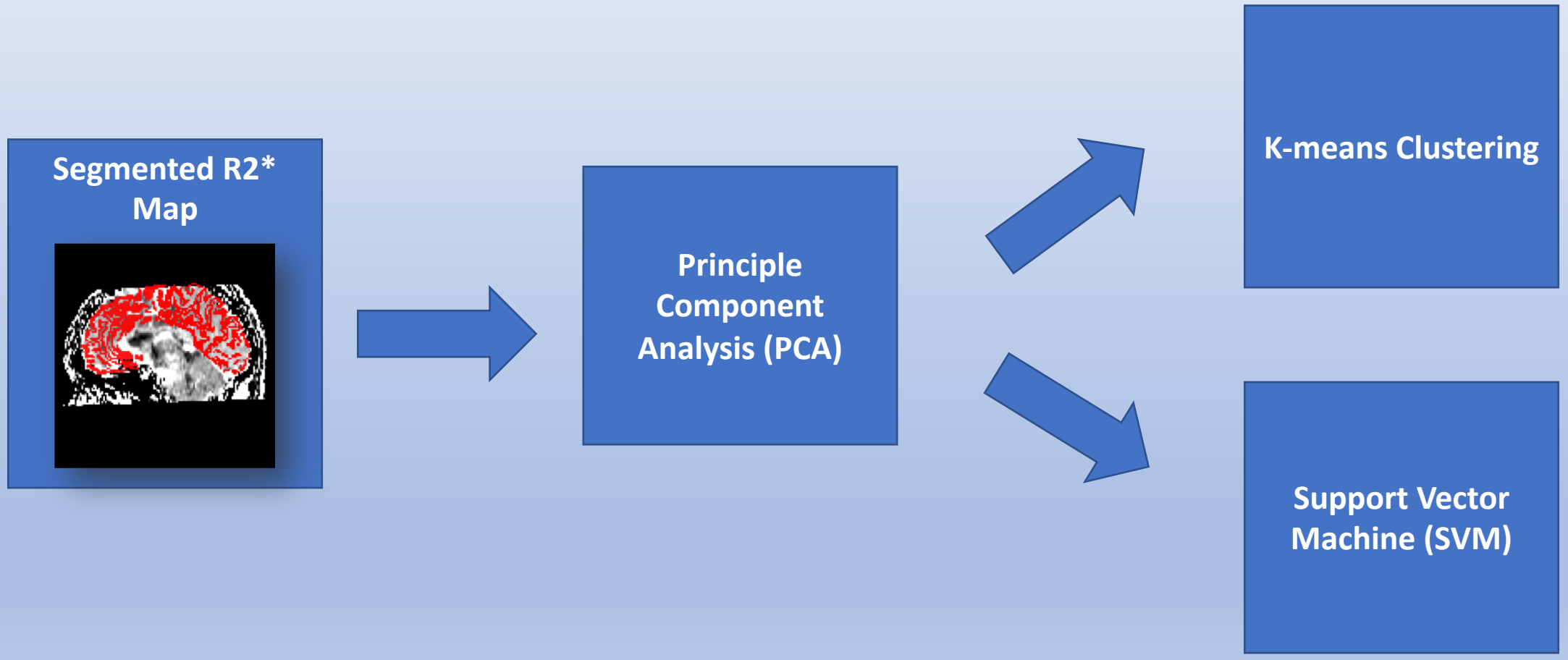
R2* Distribution in ROI

- Minor visual differences in R2* distribution between welders and controls in each ROI
  - T-tests: no statistically significant differences
  - (P-value > 0.05) between controls and welders in the 10 ROIs we chose.
- There were apparent right skews for nearly all ROIs in R2*.
  - higher R2* values in certain voxels

Figure 3. R2* Distribution in ROI



New Methods


Segmented R2* Map
Principle Component Analysis (PCA)
K-means Clustering
Support Vector Machine (SVM)

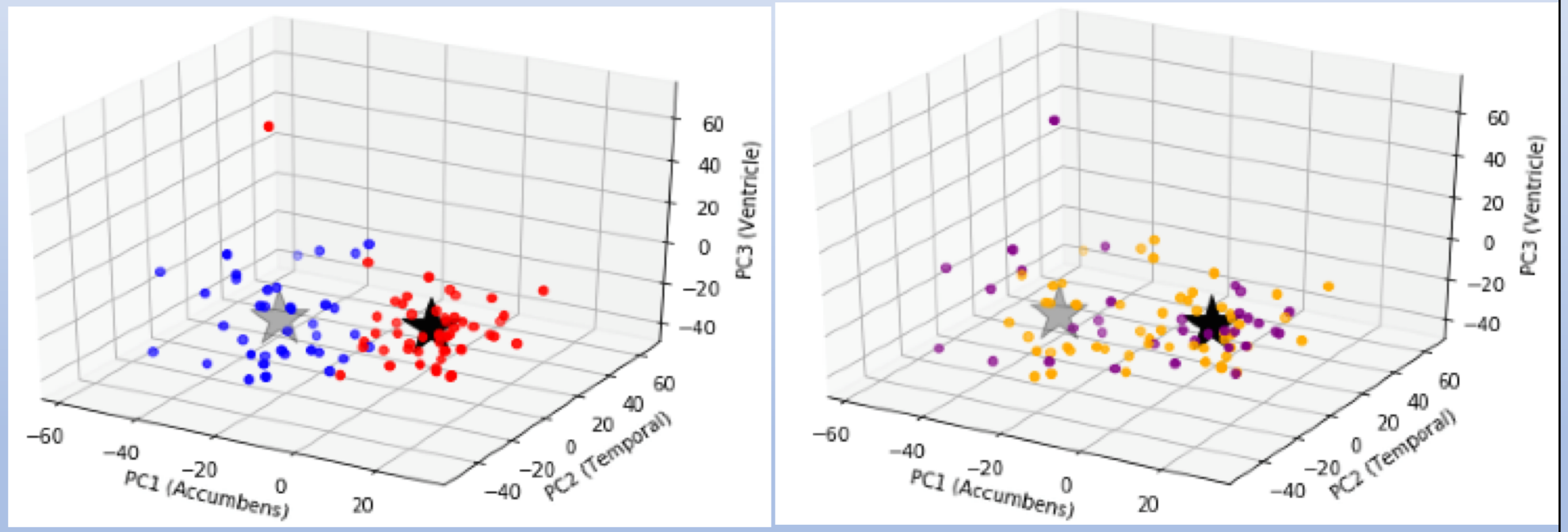
PCA Results

Table 1 PCA Results for Whole-Brain R2*				
Statistic	# PCs for 90% variance	PCA 1	PCA 2	PCA 3
		Top ROIs	Top ROIs	Top ROIs
Median	28	l.h. (G) Subcallosal l. Accumbens r.h. (G) Subcallosal	l.h. (S) suborbital r.h. (G) rectus r.h. (S) orbital medial olfactary	Optic chiasm r. inferior lateral ventricle l.h. (G) subcallosal
Ninety	31	l. Accumbens l.h. (G)Subcallosal r. Accumbens	l.h. collateral transverse anterior (S) l.h. suborbital (S)l r.h. suborbital (S)	r.h. collateral transverse anterior r.h. temporal inferior (S) r.h. temporal inferior (G)
Skew	45	r.h. (S) frontal inferior r.h. (S) orbital lateral l.h. frontal inferior Opercular	l.h. (S) occipital superior and transversal r.h. (S) occipital anterior l.h. (S) occipital middle and Lunatus	l.h. (S) orbital lateral r.h. (S) occipital anterior r.h. (S) occipital superior and transversal
lh = Left Hemisphere, rh = Right Hemisphere, S = Sulcus, G = Gyrus				

K-means clustering

Fig. 4 Median

4a 4b

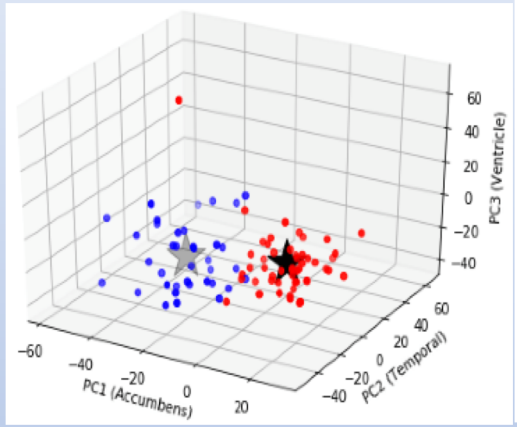


- Cluster 1
- Cluster 2
- Welder
- Control

K-means clustering

Fig. 4 Median

4a



4b

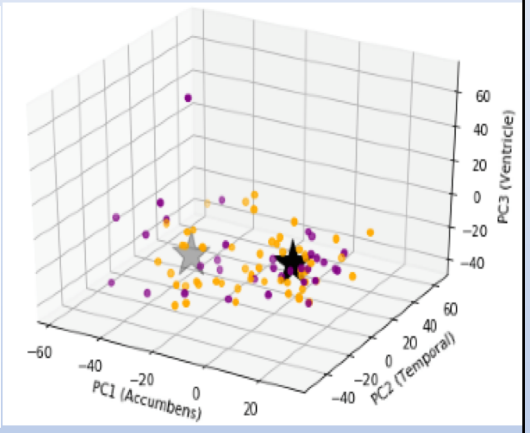
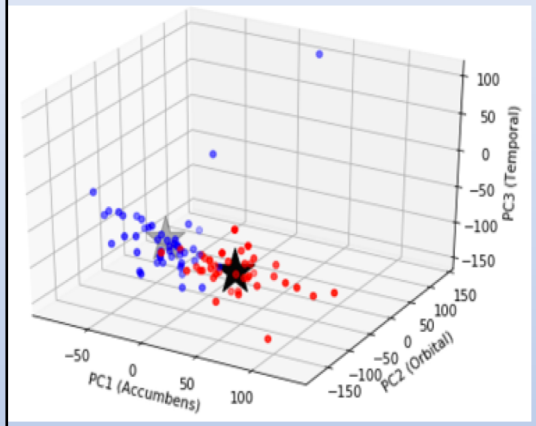


Fig. 5 Ninety

5a



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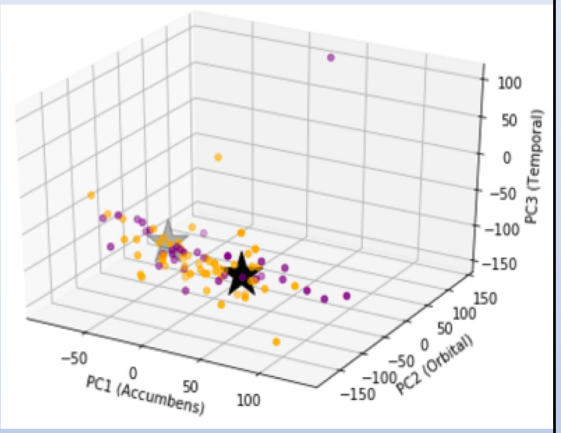
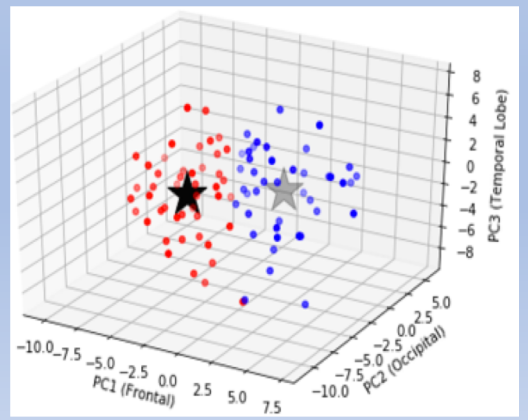


Fig. 6 Skew

6a



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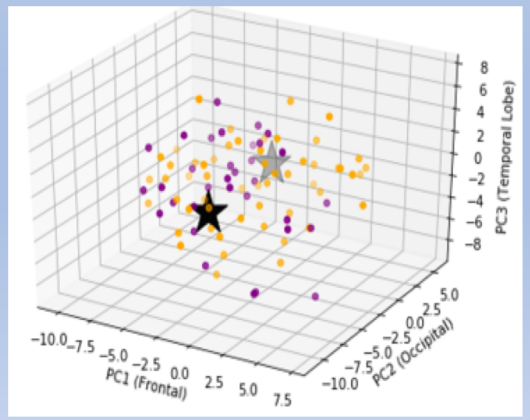

- Cluster 1
- Cluster 2
- Welder
- Control

Support Vector Machine (SVM)

- SVM models a hyperplane boundary that separates data into two categories
- SVM with a linear kernel could not distinguish between welders or controls better than chance (50% accuracy) for models using median, 90th percentile, or skew

Table 2. SVM accuracies for chosen statistics					
	Median	Ninety	Skew	Max	Mean
Accuracy	0.49	0.42	0.54	0.54	0.49

Conclusions for new methods

- While there were visible differences between groups when assessing R2* distribution, t-tests showed no statistically significant differences
- PCA significantly narrowed the number of PCs needed to explain 90% of variance in the data.
  - Median, ninety, and skew had PCs of 28, 31, and 45, respectively.
- K-means clustering and SVM were unable to differentiate between groups effectively.
  - Null results suggest that R2*, and thus brain Fe accumulation, cannot distinguish these groups.
- This provides some evidence that measures of Mn accumulation shown in previous work is caused by elevated Mn brain levels and are not confounded by an elevation of Fe levels.

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